

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

Please amend the paragraph beginning on page 1, line 13, as follows:

In living bodies, hemoglobins in red blood cells are responsible for oxygen transport. There have been reported many researches on reproduction of an oxygen-transport function similar to that of an iron(II) protoporphyrin complex that is an oxygen-binding pocket for hemoglobin, by use of various synthetic compounds. For example, pioneering reports include J.P. Collman, Acc. Chem. Res., 10, 265 (1977), and F. Basolo, B. M. Hoffman, J. A. Ibers, Ibid, 8, 384 (1975). In particular, known as an iron (II) Porphyrin complex that can form a stable oxygen complex under room temperature is 5,10,15,20-tetrakis ($\alpha,\alpha,\alpha,\alpha$ -o-pival-amidophenyl) porphyrin iron(II) complex (hereinafter referred to as a "FeTpivPP complex") (J. P. Collman, et al., J. Am. Chem. Soc., 97, 1427 (1975). The FeTpivPP complex can reversibly bind or release molecular oxygen at room temperature in the presence of an axial base (such as 1-alkylimidazole, 1-alkyl-2-methylimidazole, or a derivative of pyridine) in an organic solvent such as benzene, toluene, dichloromethane, N, N-dimethylformamide, tetrahydrofuran or the like. However, when the FeTpivPP complex is intended to be used

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in the living body as an artificial oxygen carrier (an oxygen infusion) that can exhibit the oxygen transport function in stead of hemoglobin, it is essential for the FeTpivPP complex to have an ability to bind or release oxygen under the physiological conditions (i.e., at pH 7.4, Temperature < 40 °C in physiological saline). The present inventors have succeeded in realizing oxygen infusions that can reversibly bind and release oxygen even under the physiological conditions by making active use of minute hydrophobic environments constructed in the vicinity of oxygen coordinating sites along with solubilization of the FeTpivPP complex in water, which are achieved by various methods such as, for example, a method for embedding the FeTpivPP complex or their analogues in bilayer membrane endoplasmic reticula comprising phospholipids (Dalton Trans., 1984, 1147, ~~JP S58-21371(A)~~; JP S58-213711(A)); a method for enclosing or covering the FeTpivPP complex with micro spheres comprising guttate oil globules (E. Tsuchida et al., Biochem. Biophys. Acta., 1108, 253-256 (1992), ~~JP H06-264641(A)~~; H06-263641(A)); a method of self-assembly by inducing formation of covalent bonds with amphipathic substituents (JP H06-92966(A)); and a method for enclosing serum albumin in hydrophobic domains (JP H08-301873(A)). Further, the inventors have proved that these oxygen infusions have an ability to sufficiently transport

oxygen even when administered to the living body (E. Tsuchida et. al., Artif. Organs Today, 5, 207-215 (1996)).

Please amend the paragraph beginning on page 3, line 11, as follows:

As mentioned above, in order to allow the FeTpivPP complex to exert reversible oxygen binding and releasing properties, it is necessary to externally add a basic axial ligand in an excess number of moles to the liquid. The present inventors have realized a system that can produce stable oxygen complex without addition of any basic axial ligand, by incorporating, for example, an alkyl imidazole derivative or an alkyl histidine derivative as a substituent into molecules of the iron(II) porphyrin complex to form a covalent bond therewith (~~JP-H05-85141(A)~~). Japanese Patent Application No. H05-85141(A) or JP H06-271577(A)). Some of the imidazole derivatives, which have been widely used as an axial base, have medicinal properties, but they are mostly highly toxic to the body tissues. Further, if the used carrier is phospholipid endoplasmic reticulum, lipido microspheres or albumin, the excessively coexisted imidazole derivative may be a factor contributing to destabilization of the morphologic feature. As a way to minimize the added amount of the axial base, the inventors had

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no choice but to incorporate the imidazole derivative into molecules of the iron(II) porphyrin complexes. Of course, it has been continuously and experimentally proved that the resultant modified iron(II) porphyrin complexes function as oxygen carriers that can be administered to the living bodies (E. Tsuchida et al., Bioconjugate Chem., 11, 46-50 (2000)).

Please amend the paragraph beginning on page 14, line 17, as follows:

The porphyrin metal complexes of the general formula (II) are disclosed, for example, in T. G. Traylor et al., J. Am. Chem. Soc., 101, 6716-6731 (1979), ~~JP S58-10388(A)~~ JP S58-10388(B) and JP S60-17326(A), except for those in which R8 is alkylamino. Synthesis of the porphyrin metal complexes of the general formula (II) in which R8 is alkylamino are disclosed in examples mentioned below.